IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Gustafsson et al.

Application No.: 10/629,351

Filed: July 29, 2003

Title: METHODS, SYSTEMS, AND SOFTWARE
FOR IDENTIFYING FUNCTIONAL
BIOMOLECULES

Attorney Docket No.:
MXGNP004X1/0311.310

Examiner: UNASSIGNED

Group: 1645

[Stamp: OIPE JUN 0 1 2004 US PATENT & TRADEMARK OFFICE]

INFORMATION DISCLOSURE STATEMENT
37 CFR §§1.56 AND 1.97(b)

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

The references listed in the attached PTO Form 1449, copies of which are attached, may be material to examination of the above-identified patent application. Applicants submit these references in compliance with their duty of disclosure pursuant to 37 CFR §§1.56 and 1.97. The Examiner is requested to make these references of official record in this application.

This Information Disclosure Statement is not to be construed as a representation that a search has been made, that additional information material to the examination of this application does not exist, or that these references indeed constitute prior art.

This Information Disclosure Statement is: (i) filed within three (3) months of the filing date of the above-referenced application, (ii) believed to be filed before the mailing date of a first Office Action on the merits, or (iii) believed to be filed before the mailing of a first Office Action after the filing of a Request for Continued Examination under §1.114. Accordingly, it is believed that no fees are due in connection with the filing of this Information Disclosure Statement. However, if it is determined that any fees are due, the Commissioner is hereby authorized to charge such fees to Deposit Account 500388 (Order No. MXGNP004X1).
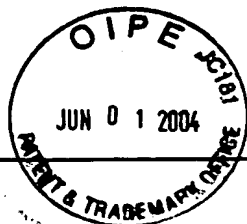
Respectfully submitted,

BEYER WEAVER & THOMAS, LLP

Jeffrey K. Weaver
Registration No. 31,314

P.O. Box 778
Berkeley, CA 94704-0778

Other Documents

Examiner Initial	No.	Author, Title, Date, Place (e.g. Journal) of Publication
	C1	Hellberg et al., "The Prediction of Bradykinin Potentiating Potency of Pentapeptides. An Example of a Peptide Quantitative Structure-Activity Relationship," Acia Chemica Scandinaviea B 40, pp. 135-140, 1988
	C2	Bucht et al., "Optimising the Signal Peptide for Glycosyl Phosphatidylinositol Modification of Human Acetylcholinesterase Using Mutational Analysis and Peptide-Quantitative Structure-Activity Relationships," Biochimica et Biophysica Acta 1431, pp. 471-482, 1999
	C3	Sandberg et al., "Engineering Multiple Properties of a Protein by Combinatorial Mutagenesis," Proc. Natl. Acad. Sci. USA, Vol. 90, pp. 8367-8371, September 1993
	C4	Wrede et al., "Peptide Design Aided by Neural Networks: Biological Activity of Artificial Signal Peptidase I Cleavage Sites," Biochemistry, 37, pp. 3588-3593, 1998
	C5	Jill Damborsky, "Quantitative Structure-Function and Structure-Stability Relationships of Purposely Modified Proteins," Protein Engineering, Vol. 11, no. 1, pp. 21-30, 1998
	C6	Hellberg, et al., "Peptide Quantitative Structure–Activity Relationships, a Multivariate Approach," J. Med Chem, 30: pp 1126-1195, 1987
	C7	Sandberg et al., "New Chemical Descriptors Relevant for the Design of Biologically Active Peptides. A Multivariate Characterization of 87 Amino Acids," J. Med Chem., 41, pp. 2481-2491, 1998
	C8	Casari et al., "A Method to Predict Functional Residues in Proteins," Nat. Struct Biol., 2, pp. 171-178, 1995
	C9	Suzuki et al., "A Method for Detecting Positive Selection at Single Amino Acid Sites," Mol. Biol. Evol. 16 (10): pp. 1315-1328, 1999
	C10	Benner et al., "Amino Acid Substitution During Functionally Constrained Divergent Evolution of Protein Sequences," Protein Engineering, Vol. 7, No. 11, pp. 1323-1332, 1994

Form 1449 (Modified)	Atty Docket No.	Application No.:
	MXGNP004X1/0311.310	10/629,351
Information Disclosure	Applicant:	
Statement By Applicant	Gustafsson et al.	
	Filing Date	Group
(Use Several Sheets if Necessary)	July 29, 2003	1645

	C11	Wu et al., "Discovering Empirically Conserved Amino Acid Substitution Groups in Databases of Protein Families," Proc. Int. Conf. Intell. Syst. Mol. Biol., 4, pp. 230-240, 1996
	C12	Adenot et al., "Peptides Quantitative Structure-Function Relationships: An Automated Mutation Strategy to Design Peptides and Pseudopeptides from Substitution Matrices," Journal of Molecular Graphics and Modelling, 17, pp. 292-309, 1999
	C13	Norinder et al., "A Quantitative Structure-Activity Relationship Study of Some Substance P-Related Peptides," J. Peptide Res., 49, pp. 155-162, 1997
	C14	Sandberg, "Deciphering Sequence Data a Multivariate Approach," Ph.D Thesis, Umea: Umea University, 78 pages, 1997
	C15	Eriksson et al., "Peptide QSAR on Substance P Analogues, Enkephalins and Bradykinins Containing L-and D-Amino Acids," Acta Chemica Scandinavica, 44, pp. 50-56, 1990
	C16	Ufkes eta l., "Further Studies on the Structure-Activity Relationships of Bradykinin-Potentiating Peptides," European Journal of Pharmacology, 79, pp. 155-158, 1982
	C17	Dobrynin et al., "Synthesis of Model Promoter for Gene Expression in Escherichia Coli," Symposium Series No. 7, pp. 365-376, 1980
	C18	Skinner et al., "Potential Use of Additivity of Mutational Effects in Simplifying Protein Engineering," Proc. Natl. Acad. Sci., Vol. 93, pp. 10753-10757, 1996
	C19	Lathrop et al., "Global Optimum Protein Threading with Gapped Alignment and Empirical Pair Score Functions," J. Mol. Biol., 255, pp. 641-665, 1996
	C20	Hellberg et al., "A Multivariate Approach to QSAR," Ph.D. Thesis, Umea, Sweden: University of Umea: 1986
	C21	Nambier et al., "Total Synthesis and Cloning of a Gene Coding for the Ribonuclease S Protein," Science, 223: 1299-1301, 1984
	C22	Lin et al., "Functional Expression of Horseradish Peroxidase in E. Coli by Directed Evolution," Biotechnol. Prog, 15: 467-471, 1999
	C23	Lathrop R.H., "The Protein Threading Problems with Sequence Amino Acids Interaction Preference is NP-Complete," Protein Eng., 7:1059-1068, 1994
	C24	Hanes et al., "In Vitro Selection and Evolution of Functional Proteins by Using Ribosomes Display," Proc. Natl. Acad. Sci. USA, 94: 4937-4942, 1997
	C25	Wells et al., "Rapid Evolution of Peptide and Protein Binding Properties in vitro," Curr Opin Biotechnol, 3:355-362, 1992

	C26	Johnson et al., "The Traveling Salesman Problem: A Case Study in Local Optimization," In Local Search in Combinatorial Optimization, Edited by Aarts et al., John Wiley & Sons Ltd., 21-310, 1997
	C28	Jonsson et al., "Quantitative Sequence-Activity Models (QSAM) – Tools for Sequence Design," Nucleic Acids Res., 21:733-739, 1993
	C29	Geladi et al., "Partial Least Squares Regression: A Tutorial," Anal Chim Acta, 168: 1-17, 1986
	C30	Holowachuk et al., "Efficient Gene Synthesis by Klenow Assembly/Extension-Pfu Polymerase Amplification (KAPPA) of Overlapping Olingonucleotides," PCR Methods Appl, 4:299-302, 1995
	C31	Hellberg et al., "Minimum Analogue Peptide Sets (MAPS) for Quantitative Structure-Activity Relationships," Int J Pept Protein Res, 37:414-424, 1991
	C32	Mee et al., "Design of Active Analogues of a 15-Residue Peptide Using D-Optimal Design, QSAR and a Combinatorial Search Algorithm," J Pept Res, 49:89-102, 1997
	C33	Schneider et al., "Peptide Design by Artificial Neural Networks and Compouter-Based Evolutionary Search," Proc Natl Acad Sci USA, 95:12179-12184, 1998
	C34	Sjostrom et al.," Signal Peptide Amino Acid Sequences in Escharichla Coli Contain Information Related to Final Protein Localization, A Multivariate Data Analysis," EMBO, 6:823-891, 1987
	C35	Patel et al., "Patenting Computer-Designed Peptides," Journal of Computer-Aided Molecular Design, 12:543-556, 1998
	C36	Aita et al., "Theory of Evolutionary Molecular Engineering Through Simultaneous Accumulation of Advantageous Mutations," J. Theor. Biol., 207:543-556, 2000
	C37	Darius et al., "Simulated Molecular Evolution of Computer Generated Artifacts?," Biophysical Journal, 67:2120-2122, 1994
	C38	Singh et al., "Application of Genetic Algorithms to Combinatorial Synthesis: A Computational Approach to Lead Identification and Lead Optimization," J.Am. Chem. Soc., 118:1669-1676, 1996
	C39	Aita et al., "Analysis of Local Fitness Landscape with a Model of the Rough Mt. Fuji-Type Landscape: Application to Prolyl Endopeptidase and Thermolysin," Biopolymers. Vol. 54, pp. 64-79, Accepted January 14, 2000
	C40	Gogos et al., "Assignment of Enzyme Substrate Specificity by Principal Component Analysis of Aligned Protein Sequences: An Experimental Test Using DNA Glycosylase Homologs," Proteins: Structure, Function, and Genetics, 40, pp. 98-105, 2000

	C41	"Vector NTI Suite 7.0 User's Manual (portion) describing software believed to be available prior to February 1, 2000
	C42	Tobin et al., "Directed Evolution: The 'Rational' Bases for 'Irrational' Design," Curr. Opin Struct Biol., 10:421-427, 2000
	C43	van Regenmortel, M.H., "Are There Two Distinct Research Strategies for Developing Biologically Active Molecules: Rational Design and Empirical Selection?", J. Mol. Recognit, 13:1-4, 2000
	C44	Ryu DD et all, "Recent Progress in Biomolecular Engineering," Biotechnol Prog., 16:2-16, 2000
	C45	Gustafsson et al., "Exploration of Sequence Space for Protein Engineering," J. Mol. Recognit, 14:308-314, 2001
	C46	Glieder et al., "Laboratory Evolution of a Soluble, Self-Sufficient, Highly Active Alkaline Hydroxylase," Nat Biotechnol, 20:1135-1139, 2002
	C47	Lehman et al., "Exchanging the Active Site Between Phytases for Altering the Functional Properties of the Enzyme," Protein Sci, 9:1866-1872, 2000
	C48	Kwasigroch et all, "PoPMuSiC, Rationally Designing Point Mutations in Protein Structures," Bioinformatics, 16:1701-1702, 2002
	C49	Tangri et al., "Rationally Engineered Proteins or Antibodies with Absent or Reduced Immunogenicity," Curr Med Chem, 9:2191-2199, 2002
	C50	Pierce et al., "Protein Design is NP-Hard," Protein Eng, 15:779-782, 2002
	C51	Ness et al., "Molecular Breeding: The Natural Approach to Protein Design," Adv Protein Chem, 55:261-292, 2000
	C52	Lehmann et al., "The Consensus Concept for Thermostability Engineering of Proteins: Further Proof of Concept," Protein Eng., 15:403-411, 2002
	C53	Dimmic et al., "rtREV: An Amino Acid Substitution Matrix for Inference of Retrovirus and Reverse Transcriptase Phylogeny," J. Mol Evol, 55:65-73, 2002
	C54	Aita et al., "A Cross-Section of the Fitness Landscape of Dihydrofolate Reductase," Protein Eng, 14:633-638, 2001
	C55	Strom et al., "Important Structural Features of 15-Residue Lactoferricin Derivatives and Methods for Improvement of Antimicrobial Activity," Biochem Cell Biol, 80:65-74, 2002
	C56	Choulier et al., "QSAR Studies Applied to the Prediction of Antigen-Antibody Interaction Kinetics as Measured by BIACORE," Protein Eng, 15(5):378-382
	C57	Hoover et al., "DNAWorks: An Automated Method for Designing Oligonucleotides for PCR-Based Gene Synthesis, " Nucleic Acids Res, 30:E43, 2002

	C58	Abecassis et all, "High Efficiency Family Shuffling Based on Multi-Step PCR and In vivo DNA Recombination in Yeast: Statistical and Functional Analysis of a Combinatorial Library Between Human Cytochrome P460 1A1 and 1A2," Nucleic Acids Res., 28:E88, 2000
	C60	Aita et al., "Surveying a Local Fitness Landscape of a Protein with Epistatic Altee for the Study of Directed Evolution," Biopolymers, 64:95-106, 2002
	C61	Prusis et al., "Proteo-chemometrics Analysis of MSH Peptide Binding to Melancortin Receptors," Protein Eng, 15:305-311, 2002
	C62	Prusis et al., "PLS Modeling of Chimeric MS04/MSH-Peptide and MC1/MC3-Receptor Interaction Reveals a Novel Method for the Analysis of Ligand-Receptor Interactions," Biochim Biophys Acta, 1544(1-2):350-357, 2001
	C63	Lu et al., "Predicting the Reactivity of Proteins from Their Sequence Alone: Kazal Family of Protein Inhibitors of Serine Proteinases," Proc Natl Acad Sci USA, 98(4):1410-1415, 2001
	C64	Schein et al., "Chloroplast Transit Peptide Prediction: A Peek Inside the Black Box," Nucleic Acids Res, 29:E82, 2001
	C65	Fariselli et al., "Prediction of Protein-Protein Interaction Sites in Heterocomplexes with Neural Networks," Eur J Biochem, 269:1356-1361, 2002
	C66	Fariselli et al., "Prediction of Contact Maps with Neural Networks and Correlated Mutations," Protein Eng, 14(11): 835-843, 2001
	C67	Marvanova et al., "Biochemical Characterization of Broad-Specificity Enzymes Using Multivariate Experimental Design and a Colorimetric Microplate Assay: Characterization of the Haloalkane Dehalogenase Mutants," J. Microbiol Methods, 44:14-157, 2001
	C68	Looger et al., "Computational Design of Receptor and Sensor Proteins with Novel Functions, Nature, 423:185-190, 2003
	C69	Govindarajan et al., "Systematic Variation of Amino Acid Substitutions for Stringent Assessment of Pairwise Covariation," J. Mol. Biol, 328:1061-1069, 2003
	C70	del Sol Mesa et al., "Automatic Methods for Predicting Functionality Important Residues," J Mol Biol, 326:1289-1302, 2003
	C71	Benos et al., "Additivity in Protein-DNA Interactions: How Good an Approximation is it?" Nucleic Acids Res 30(20): 4442-51, 2002
	C72	Bogarad et al., "A Hierarchical Approach to Protein Molecular Evolution," Proc Natl Acad Sci USA, 96:2591-2595, 0666

	C73	Carlsen et al., "QSAR's Based on Partial Order Ranking," SAR QSAR Environ Res, 13(1): 153-165, 2002
	C74	Crameri et al., "DNA Shuffling of a Family of Genes from Diverse Species Accelerates Directed Evolution," Nature, 391:288-291, 1998
	C75	Dill K.A., "Additivity Principles in Biochemistry," J Biol Chem, 272(2): 701-704, 1997
	C76	Distefano et al., " Quantifying Beta-Sheet Stability by Phage Display," J Mol Biol, 322(1):179-188, 2002
	C77	Hayes et al., "Combining Computational and Experimental Screening for Rapid Optimization of Protein Properties," Proc Natl Acad Sci USA, 99(25):15926-15931, 2002
	C78	Kell, D.B., "Metabolomics and Machine Learning: Explanatory Analysis of Complex Metabolome Data Using Genetic Programming to Produce Simple, Robust Rules," Mol Biol Rep, 29(1-2): 237-241, 2002
	C79	Koshi et al., "Context-Dependent Optimal Substitution Matrices," Protein Eng, 8:641-645, 1995
	C80	Koshi et al., "Mutation Matrices and Physical-Chemical Properties: Correlations and Implications," Proteins 27(3):336-344, 1997
	C81	Lahr et al., "Patterned Library Analysis: A Method for the Quantitative Assessment of Hypotheses Concerning the Determinants of Protein Structure," Proc Natl Acad Sci USA, 96(26):14860-14865, 1999
	C82	Lapinsh et al., "Classification of G-Protein Coupled Receptors by Alignment Independent Extraction of Principal Chemical Properties of Primary Amino Acid Sequences," Protein Sci 11(4):795-805
	C83	Lapinsh et al., "Development of Proteo-Chemometrics: A Novel Technology for the Analysis of Drug-Receptor Interactions," Biochim Biophys Acata, 1525(1-2): 180-190
	C84	Lapinsh et al., "Protechemometrics Modeling of the Interaction of Amine G-Protein Coupled Receptors with a Diverse Set of Ligands," Mol Pharmacol 61(6): 1465-1475, 2002
	C85	Lapinsh et al., "QSAR and Proteo-Chemometric Analysis of the Interaction of a Series of Organic Compounds with Melanocortin Receptor Subtypes," J Med Chem, 46(13): 2572-2579, 2003
	C86	Lee et al., "Mathematical Modelling of Inset Neuropeptide Potencies. Are Quantitatively Predictive Models Possible," Insect Biochem Mol Biol, 30(10): 899-907, 2000

	C87	Lehman et al., "Engineering Proteins Thermostability: the Use of sequence Alignments Versus Rational Design and Directed Evolution," Current Opinion in Biotechnology 12:371-375, 2001
	C88	Linusson et al., Statistical Molecular Design of Building Blocks for Combinatorial Chemistry," J Med Chem, 43(7): 1320-1328, 2000
	C89	Matsuura eta l., "Nonaddivity of Mutational Effects on the Properties of Catalasa I and its Application to Efficient Directed Evolution," Protein Eng, 11(9): 789-795, 1998
	C90	Nakai et al., "Structure Modification and Functionality of Why Proteins: Quantitative Structure-Activity Relationship Approach," J Dairy Sci, 68(10):2763-2772, 1985
	C91	Nakai et al., "Recent Advances in Structure and Function of Food Proteins: QSAR Approach," Crit Rev Food Sci Nutr, 33(6):477-499
	C92	Ness et al., "Synthetic Shuffling Expands Functional Protein Diversity by Allowing Amino Acids to Recombine Independently," Nat Biotechnol, 20(12):1251-1255, 2002
	C93	Niggemann et al., "Exploring Local and Non-Local Interactions for Protein Stability by Structural Motif Engineering," J Mol Biol, 296(1):181-195, 2000
	C94	Nikolova et al., "Semirational Design of Active Tumor Suppressor p53 DNA Binding Domain with Enhanced Stability," Proc Natl Acad Sci USA, 95(25): 14675-14680, 1998
	C95	Reymond et al., "Substrate Arrays as Enzyme Fingerprinting Tools," Chembiochem, 3(8):701-708, 2002
	C100	Sadowski et al., "Automated Generation and Refinement of Protein Signatures: Case Study with G-Protein Coupled Receptors," Bioinformatics, 19(6(: 727-734, 2003
	C101	Shaw et al., "Predicting Amino Acid Residues Responsible for Enzyme Specificity Solely from Protein Sequences," Biotechnol Bioeng, 79(3): 295-300, 2002
	C102	Sheridan et al., "Designing Targeted Libraries with Genetic Algorithms," J Mol Graph Model, 18(4-5): 320-345, 525, 2000
	C103	Siebert, K.J., "Quantitative Structure-Activity Relationship Modeling of Peptide and Protein Behavior as a Function of Amino Acid Composition," J Agric Food Chem, 49(2): 851-858, 2001
	C104	Siebert, K.J., "Modeling Protein Function Properties from Amino Acid Composition," J Agric Food Chem, 51(26): 7792-7797, 2003
	C105	Soyer et al., "Using Evolutionary Methods to Study G-Protein Coupled Receptors," Pac Symp Biocomput: 625-636, 2002

	C106	Steipe, B., "Evolutionary Approaches to Protein Engineering," Curr Top Microbiol Immunol, 243: 55-86, 1999
	C107	Umeno et al., "Evolution of the C30 Carotenoid Synthase CrtM for Function in a C40 Pathway," J Bacteriold 184(23): 6690-6699, 2002
	C108	Veraverbeke et al., "Wheat Protein Composition and Properties of Wheat Glutenin in Relation to Breadmaking Functionality," Crit Rev Food Sci Nutr, 42(3): 179-208, 2002
	C109	Wahler et al., "Enzyme Fingerprints by Fluorogenic and Chromogenic Substrate Arrays," Angew Chem Int Ed Engl,, 40(23): 4457-4460, 2001
	C110	Wahler et al., "Enzyme Fingerprints of Activity, and Stereo and Enantioselectivity from Fluorogenic and Chromogenic Substrate Arrays," Chemistry, 8(14): 3211-3228, 2002
	C111	Wang et al., "Designing Gene Libraries from Protein Profiles for Combinatorial Protein Experiments," Nucleic Acids Res, 30(21): e120, 2002
	C112	Wells, J.A., "Additivity of Mutational Effects in Proteins," Biochemistry, 29(37): 8509-8517, 1990
	C113	Wikberg et al., "Melanocortin Receptors: Ligands and Protechemometrics Modeling," Ann NY Acad Sci, 994:21-26, 2003
	C114	Martin et al., "Measuring Diversity: Experimental Design of Combinatorial Libraries for Drug Discovery," J. Med. Chem. 38, 1431-1436, 1995
	C115	Sheridan et al., " Using a Genetic Algorithm to Suggest Combinatorial Libraries," J. Chem. Inf. Compu. Sci., 35, 310-320, 1995
	C116	D.K. Agrafiotis, "Multiobjective Optimization of Combinatorial Libraries," IBM J. Res & Dev., Vol, 45, No. 3, 545-566, 2001
Examiner		Date Considered	

Examiner: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.